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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,988	06/13/2001	Charles R. Cantor	25491-2408	5954

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HELLER EHRMAN WHITE & MCAULIFFE LLP
4350 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122-1246

EXAMINER

CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/880,988

Applicant(s)

Cantor

Examiner

Arun Chakrabarti

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Apr 4, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s): _____
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: _____
- Claim(s) objected to: _____
- Claim(s) rejected: 1-8, 10-20, and 25-45
- Claim(s) withdrawn from consideration: _____
8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____

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Applicant's request for reconsideration has been considered but does not place the application in condition for allowance because of the following reasons:

A) In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Canrad et al as Canrad et al states, "The use of hairpin primer makes it possible to use basic conditions for deprotection of the 3' hydroxyl compatible with a repetition of the procedure without addition of a primer at each step of the indirect determination of a nucleotide inserted. In fact, rehybridization of the primer occurs intramolecularly and immediately (Column 4, line 66 to column 5, line 4)". Similar logic is applicable to other combinatory references as well.

B) In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

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C) Applicant then argues the 103 rejection is improper because it lacks a reasonable expectation of success.

With regard to the “lacks a reasonable expectation of success” argument, The MPEP 2143.02 states

“Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed

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enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.).”

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Brennan reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different nucleotides were actually experimentally studied, identified and found to be functional (Abstract, Column 5, line 25 to Column 6, line 8, and Examples 1-4, and Schemes D and E). This evidence of functionality trumps the attorney arguments, which argues that Brennan reference is an invitation to research, since Brennan steps beyond research and shows the functional product.

D) Applicant argues that Brennan reference does not teach the mass-matched nucleotide and determination of mass of an extension product of the claimed invention. Applicant argues that the word “mass-matched nucleotide” and the “mass of an extension product” was not found in Brennan reference and only the word “mass of the combustion product of a nuclide label” is found. Applicant argues that because Brennan has a preferred embodiment of determination of mass of the combustion product of a nuclide label, Brennan is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states “Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 169 USPQ 423 (CCPA 1971).” MPEP 2123 also states “A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft

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Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989).” It is clear that simply because Brennan has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Brennan reference uses mass of the combustion product of a nuclide label, the properties of mass-matched nucleotide and mass of an extension product are inherently present in this chemically and structurally identical molecule. For example, Brennan teaches that such method can be used to for detecting different nucleotide base compositions in a population of nucleic acids having identical length and different base compositions with respect to the difference of a single base (Column 11, lines 1-38, and Figures 1-2). Moreover, MPEP 2111 states, “Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be “given the broadest reasonable interpretation consistent with the specification”. Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)”. In the presence of “comprising” language of the claims, any additional step(s) or materials can be included (in this case, identification of nuclide labels).

E) In response to applicant's argument that Canrad reference is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977

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F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Canrad reference is clearly pertinent to the particular problem with which the applicant was concerned, which is the determination of a nucleotide inserted in a particular position of a nucleic acid.

For the reasons mentioned above, applicant's argument was not found persuasive and therefore, the amendment and request for reconsideration were not entered.


GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600